UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/767,370	01/23/2001	Jeffrey Browning	BGNA054RCE	2716

959 7590 02/10/2006

LAHIVE & COCKFIELD, LLP.
28 STATE STREET
BOSTON, MA 02109

EXAMINER	
YAEN, CHRISTOPHER H	
ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 02/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/767,370	BROWNING ET AL.	
	Examiner	Art Unit	
	Christopher H. Yaen	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8,10,11,16,26,28,29 and 37-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8,10,11,16,26,28,29 and 37-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Re: BROWNING *et al*

1. The amendment filed 11/22/2005 is acknowledged and entered into the record. Accordingly, claims 1-7,9,12-15,17-25,27, and 30-36, are canceled without prejudice or disclaimer.

2. Claims 8,10-11,16,26,28-29, and 37-51 are pending and examined on the merits.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

4. The disclosure is objected to because of the following informalities:

a. 37 CFR 1.82(d) requires the use of the assigned sequence identifier (SEQ ID No:) in all instances where the description of a patent application refers to a sequence and whenever a sequence or fragment thereof is claimed (see MPEP 2422.03). In particular, the specification receites a sequence, however no sequence identifier is present (see page 20).

Appropriate correction is required.

Claim Rejections Maintained - 35 USC § 102

5. The rejection of claims 8,26,39,42,43, 49, and now newly rejected claim 40 under 35 USC § 102(b) as being anticipated by Beutler *et al* (US Patent 5,447,851) as evidenced by InVitrogen Life Technologies Instruction Manual (*BaculoDirect™ Baculovirus Expression System* 2004; Version F:1-64; herein InVitrogen Manual) is

maintained for the reasons of record. Applicant argues that the Beutler *et al* does not teach each and every element of the claimed invention and that the reliance on the InVitrogen Manual is improper because the "extra reference" (i.e. the Invitrogen Manual) does not serve the purpose of proving that the primary reference is an enabling reference, explain a maneing of a term used in the primary reference, or show a characteristic not disclosed in the reference is inherent. Applicant further contends that the cited reference does not teach the required element of the culturing temperature as recited in the claim. Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record.

Beutler *et al* teach the construction of a TNF receptor: Ig fusion protein (termed TNF inhibitor) by culturing mammalian cells comprising an expression vector that encodes the said TNF receptor:Ig fusion protein and collecting the serum free conditioned media. The said media was then clarified on an affinity column, eluted from the column using a solution at low pH, followed by neutralization with a Tris Buffer (see Col. 21, lines 39-54, in particular). The specification on page 13 teaches that one of the means to purify "active" forms of the LT-βR:Ig fusion proteins is by using low pH. In addition, the specification also teaches that other members of the TNF receptor family suffer from the same problems similar to the LT-βR:Ig fusion protein (see page 11, lines 13-14). Thus in the absence of evidence to the contrary, the low pH elution as taught by Beutler *et al* would produce more of an "active" form of the protein because as defined by the specification, the TNF receptor family fold via similar pathways. In addition, the specification also teaches that "inactive" forms of the chimeric molecule is

part of the "flow through" and thus would, in the absence of the evidence to the contrary, be absent from the bound material eluted from the column (see page 12).

The reliance on the evidentiary reference (i.e. InVitrogen manual) was only to serve the point that the conventional culturing conditions for the baculovirus system is 27°C. However, even in the absence of disclosing the temperature, the claims as constructed are product-by-process claims. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). In the instant case, the process of making the receptor:ig fusion protein appears to be identical given similar purification steps disclosed in the specification. Thus, although the temperature at which the cells where incubated may be different, the product appears to be identical and therefore the method of making the product is immaterial in differentiating the claimed product from the prior art.

Applicant additionally argues that in addition to the cell culture supernatants, the claims also require a certain percentage of "biologically active receptor:Ig proteins" that result from the claimed culturing temperature (i.e. the lower temperatures 27°C-35°C). In particular, applicant indicates that the percentage of biologically active receptor:Ig fuson protein includes at least 70% biologically active protein. Applicant also contends that the examiner fails to make a *prima facie* case such that if one of skill in the art

followed the teachings of Beutler *et al* as evidenced by InVitrogen Manual that the claimed composition would be produced with the same "biologically active" receptor:Ig fusion protein. Applicant's arguments have been carefully considered but are not deemed persuasive to overcomes the rejection of record.

The specification of the instant application has not specifically defined the term "biologically active", instead, what the specification does define is the term "active". The term "active" as defined by the specification are those proteins capable of binding with "high affinity" (see page 9, line 7, for example). Therefore, "biologically active" proteins encompass proteins that have any biological function. Thus, Beutler *et al* teaches a chimeric protein that is "biologically active" because it is capable of (1) binding to an affinity resin via the Fc domain (see Col. 21, lines 39-54) and (2) terminating pregnancy in vivo (see col. 23, lines 27-35) through its ability to mediate functionality through the the TNF receptor. Thus, the chimeric molecule used by Beutler *et al* was 100% biologically active and therefore fulfills the limitation of at least 70% "biologically active".

Therefore, the rejection of claims under 35 USC 102(b) is maintained for the reasons of record.

Claim Rejections Maintained - 35 USC § 102

6. The rejection of claims 8,11,26,29,37-40,42-43, and 49 under 35 USC § 102(b) as being anticipated by Ashkenazi *et al* (WO 98/25967) as evidenced by the InVitrogen Manual is maintained for the reasons of record. Applicant's arguments are substantially similar to those previously argued above for the 102(b) rejection over Beutler *et al* as

evidenced by the InVitrogen Manual. Specifically, applicant indicates that Ashkenazi *et al* does not teach essential elements of the claimed invention such as the temperature and percentage of biologically active HVEM:Ig fusion proteins as claimed. Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record based on the arguments previously presented and argued above.

In particular, Ashkenazi *et al* teach that HVEM:Ig protein may be purified by numerous chromatography methods (see page 16-17). Because the specification teaches numerous means of purification using "conventional" chromatographic methods (see page 12, example 3), one of skill in the art would expect that the active forms of the HVEM:Ig fusion protein as disclosed by Ashkenazi *et al* would produce highly biologically active proteins. Thus the rejection under 35 USC 102(b) as being anticipated by Ashkenazi *et al* is maintained for the reasons of record.

Claim Rejections Withdrawn - 35 U.S.C. § 103

7. The rejection of claims under 35 USC § 103(a) as being obvious over Crowe *et al*, Kwon *et al*, or Rennert *et al*, in view of Nilsson *et al* or Beutler *et al* is withdrawn in view of the persuasive arguments set forth by the applicant in the paper filed 11/22/2005.

NEW ARGUMENTS

Claim Rejections - 35 USC § 112, 1st paragraph

8. Claims 8,10-11,16,26,28-29,,37-42,44-47, and 49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION.

Independent claims 8,16,26,37,44, and 49 recite the limitation of " at least 70% biologically active" (claims 8,26,37,44, and 49) or "at least 70% LT-b-R-Ig-fusion protein (claim 16) as part of the invention. The specification or claims as filed do not support the specific limitation of "at least 70%". The specification does however support claims wherein the percent biologically active is at least 83% (see page 18 for example). The limitation of at least 70% is not either explicitly or implicitly supported in the specification. Applicant is invited to point to clear support or specific examples of the claimed invention in the specification as-filed by referring to specific page and line number.

Claim Rejections - 35 USC § 102

9. Claim 8,10,16,26,28, and 39-51are rejected under 35 U.S.C. 102(b) as being anticipated by Degli-Esposti *et al* (J Immunol. 1997 Feb 15;158(4):1756-62, IDS 1/92002 #CO).

Degli-Esposti *et al* teach an LT-β-R-Ig fusion protein and further teach that the fusion protein can be administered to a mouse for the production of a monoclonal antibody (see page 1758). The specification of the instant application teaches that conventional chromatography methods can be used to produce "active" proteins, such methods include affinity chromatography (see page 12 of the specification), wherein the "inactive" protein flows out of the column in the flow through and only "active" protein remain bound and can be eluted by low pH buffers. Degli-Esposti *et al* followed a technique that used affinity chromatography followed by low pH elution as directed by Fanslow *et al* (J. Immunol 1992; 149:665-660, attached).

Because the term "biologically active" has not been adequately defined in the specification as filed, for the purposes of this rejection, a "biologically active" protein is that which is able to elicit an immunogenic response. In this case, Degli-Esposti *et al* uses the LT-β-R-Ig fusion protein to immunize mice for the production of a M12 monoclonal antibody. Therefore, because it was taught that the M12 antibody was produced and able to recognize both recombinant and native LT-β-R, the LT-β-R-Ig fusion protein was deemed biologically active. Moreover, because it was purified, the preparation was at least 70% "biologically" active.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H. Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher Yaen
Art Unit 1643
February 2, 2006

CHRISTOPHER YAEN
PATENT EXAMINER